IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	John A. Kink	
Serial No.:	09/095,536	Group No.: 1646
Filed:	06/10/98	Examiner: Hissong
Entitled:	**Prevention and Treatment of Sepsis**	

DECLARATION OF DR. DOUGLAS STAFFORD

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Dated: October 17, 2007 By: _____
Traci E. Light

I, Dr. Douglas Stafford, under penalty of perjury, state that:

1. I am the former President and CEO of the former assignee of the above-captioned United States Patent Application. I am familiar with the experimental data set forth in the specification. I have graduate degrees in microbiology and immunology.
2. I understand that, in a recent Office Action, the Examiner states that "One of skill in the art would not know whether the results presented in Table 5 are truly unexpected, or are merely differences due to the timing of antibody administration after LPS challenge."
3. I understand that the Examiner also asks whether "administration of anti-IFN-γ, or combined anti-IFN-γ and anti-TNF-α antibodies at 5 minutes post-challenge offer the same degree of protection as the combination of all three antibodies at 5 minutes post challenge."
4. It is important to emphasize that Table 5 shows the results from a particularly aggressive gram-negative sepsis model wherein a lethal dose of LPS is administered and followed by antibody administration (note the language in Example 5: "This model is also considered very aggressive, and the onset of septic shock is quite rapid.") The approach does NOT involve pre-mixing or pre-treatment.

5. Table 5 shows that anti-TNF-α antibodies alone (whether at 5 minutes or 15 minutes post-challenge) are not protective. Table 5 also shows that anti-IFN-γ antibodies in combination with anti-IL-6 antibodies are not protective at 5 minutes post-challenge. By contrast, the combination of anti-IL-6, anti-IFN-γ and anti-TNF-α antibodies provide complete (100%) protection at 5 minutes post-challenge. These differences are NOT due to the timing of administration, since the timing was the same (i.e. 5 minutes post-challenge).

6. Looking strictly at the data in Table 5, it is clear that the degree of results obtained with the three antibody combination, namely 100% rescue, is in sharp contrast to the results obtained with anti-TNF-α alone (where 0% was observed). Similarly, anti-IFN-γ antibodies in combination with anti-IL-6 antibodies achieved only 33% survival. Thus, there is no basis for speculating that "anti-IFN-γ, or combined anti-IFN-γ and anti-TNF-α antibodies at 5 minutes post-challenge offer the same degree of protection as the combination . . ." While such single antibodies or two antibody combinations may provide SOME protection (e.g. 33% to 50% survival), there is nothing in Table 5 to suggest that single antibodies or two antibody combinations could achieve 100% survival. Indeed, the 100% result is quite unexpected in view of the rather poor results obtained with single antibody and two antibody combinations.

7. The rigor of the test is evident from the data in Table 5. More specifically, Table 5 does show that the benefit of the three antibody combination is diminished if the timing of the administration is delayed. This underscores the point that the onset of shock is rapid.

Dated: October 16, 2007

Douglas Stafford, Ph.D.